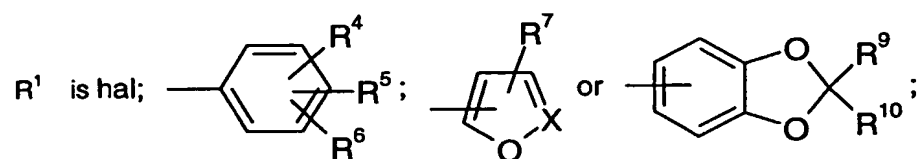


Claims

1. A quinazolinone of formula I .



wherein



X is N or CR⁸;

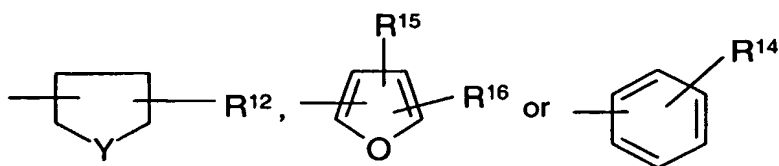
R² is hal; nitro; C₁-C₆alkylcarbonyl; C₁-C₆alkyl or C₃-C₆cycloalkyl;

R³ is C₁-C₆alkyl; C₁-C₆alkoxy or amino;

R⁴ is H; hal; hydroxy; amino; C₁-C₆alkyl-amino, di(C₁-C₆alkyl)-amino, C₁-C₆alkyl; C₁-C₆alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkyl; C₃-C₇cycloalkyl or C₃-C₇cycloalkylC₁-C₆alkoxy that may be substituted at the cycloalkyl residue by C₁-C₆alkyl; C₁-C₆alkoxycarbonyl; C₃-C₆alkenyloxy; (C₁-C₆alkyl)₂N-C₁-



-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R⁹ and R¹⁰, independently, are H or hal;

R^{11} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

R^{12} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

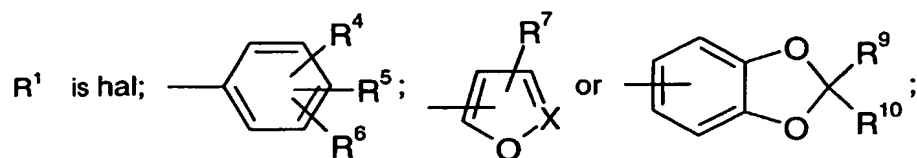
R^{13} is H or C_1 - C_6 alkyl;

R^{14} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl; and

R^{15} and R^{16} , independently, are H; hal; or C_1 - C_6 alkyl;

with the exception of the compound of formula I wherein R^1 and R^2 are both iodo or chloro and R^3 is methyl, and of the compound of formula I wherein R^1 and R^2 are both selected from fluoro and bromo and R^3 is butyl, in free base or acid addition salt form.

2. A quinazolinone of formula I according to claim 1 wherein



X is N or CR^8 ;

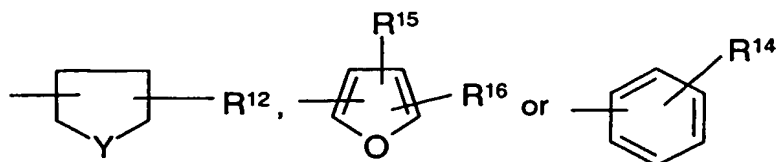
R^2 is C_1 - C_6 alkyl;

R^3 is C_1 - C_6 alkyl; C_1 - C_6 alkoxy or amino;

R^4 is H; hal; hydroxy; amino; C_1 - C_6 alkyl-amino, di(C_1 - C_6 alkyl)-amino, C_1 - C_6 alkyl; C_1 - C_6 alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkyl; C_3 - C_7 cycloalkyl or C_3 - C_7 cycloalkyl C_1 - C_6 alkoxy that may be substituted at the cycloalkyl residue by C_1 - C_6 alkyl; C_1 - C_6 alkoxycarbonyl; C_3 - C_6 alkenyloxy; $(C_1$ - C_6 alkyl) $_2$ N- C_1 -



-O-[CH_2] $_n$ -A wherein A represents



Y represents O or NR^{13} ,

and n is 0, 1, 2, 3, 4, 5 or 6;

R^5 and R^6 , independently, are H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

R^7 and R^8 , independently, are H or C_1 - C_6 alkyl;

R^9 and R^{10} , independently, are H or hal;

R^{11} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

R^{12} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

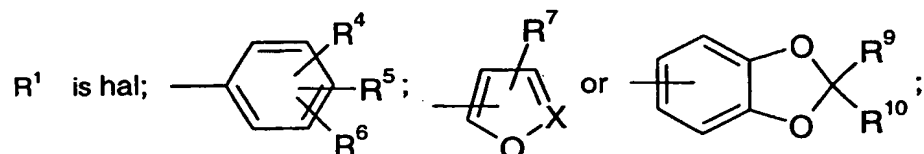
R^{13} is H or C_1 - C_6 alkyl;

R^{14} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl; and

R^{15} and R^{16} , independently, are H; hal; or C_1 - C_6 alkyl;

in free base or acid addition salt form.

3. A quinazolinone of formula I according to claim 1 or 2 wherein

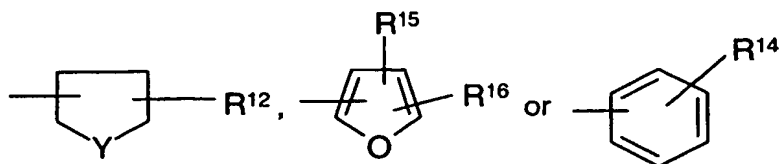


X is N or CR^8 ;

R^2 is C_1 - C_6 alkyl;

R^3 is C_1 - C_6 alkyl or amino;

R^4 is hal; hydroxy; amino; C_1 - C_6 alkyl-amino, C_1 - C_6 alkyl; C_1 - C_6 alkoxy which is unsubstituted or monosubstituted by halogen or hydroxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkyl; C_3 - C_7 cycloalkyl or C_3 - C_7 cycloalkyl C_1 - C_6 alkoxy that may be substituted at the cycloalkyl residue by C_1 - C_6 alkyl; C_1 - C_6 alkoxycarbonyl; C_3 - C_6 alkenyloxy; $(C_1$ - C_6 alkyl) $_2$ N- C_1 - C_6 alkoxy; C_1 - C_6 alkyl-sulfanyl; C_1 - C_6 alkyl-sulfanyl C_1 - C_6 alkoxy, or $-O-[CH_2]_n-A$ wherein A represents



Y represents O or NR^{13} ,

and n is 0, 1 or 2;

R^5 and R^6 , independently, are H; hal; or C_1 - C_6 alkoxy;

R^7 and R^8 , independently, are H or C_1 - C_6 alkyl;

R^9 and R^{10} , independently, are H or hal;

R^{12} is H;

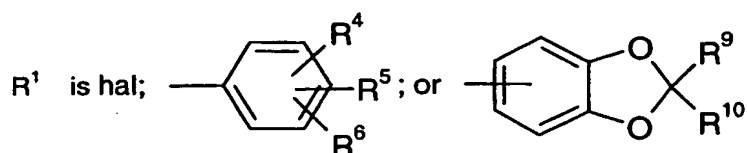
R^{13} is C_1 - C_6 alkyl;

R^{14} is H; or C_1 - C_6 alkoxy; and

R^{15} and R^{16} are H;

in free base or acid addition salt form.

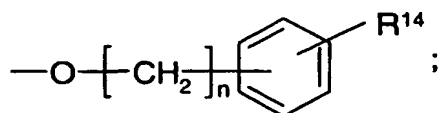
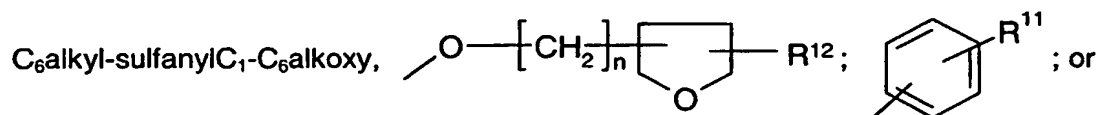
4. A compound of formula I according to claim 1 wherein



R^2 is hal; nitro; C_1 - C_6 alkylcarbonyl; C_1 - C_6 alkyl or C_3 - C_6 cycloalkyl;

R^3 is C_1 - C_6 alkyl; C_1 - C_6 alkoxy or amino;

R^4 is H; hal; hydroxy; C_1 - C_6 alkyl; C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkyl; halogeno C_1 - C_6 alkoxy; C_3 - C_7 cycloalkyl C_1 - C_6 alkoxy that may be substituted at the cycloalkyl residue by C_1 - C_6 alkyl; C_1 - C_6 alkoxycarbonyl; C_3 - C_6 alkenyloxy; $(C_1$ - C_6 alkyl) $_2$ N- C_1 - C_6 alkoxy; C_1 - C_6 alkyl-sulfanyl; C_1 -



wherein n is 0, 1, 2, 3, 4, 5 or 6;

R^5 , R^6 , R^{11} and R^{14} , independently, are H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

R^{12} is H or C_1 - C_6 alkyl; and

R^9 and R^{10} , independently, are H or hal;

with the exception of the compound of formula I wherein R^1 and R^2 are both iodo or chloro and R^3 is methyl, and of the compound of formula I wherein R^1 and R^2 are both selected from fluoro and bromo and R^3 is butyl,

in free base or acid addition salt form.

5. A compound of formula II

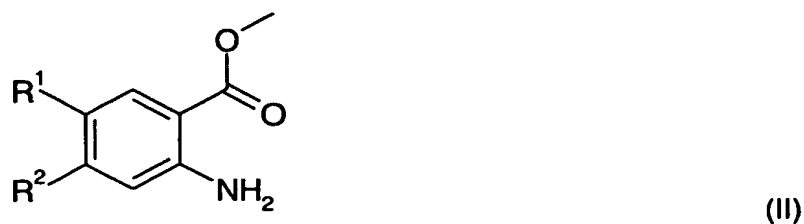


wherein

R¹ and R² are as defined in claim 1.

6. A process for the preparation of a compound of formula I as defined in claim 1, or a salt thereof, comprising the steps of

a) for the production of a compound of formula I wherein R³ is not NH₂, reacting a compound of formula II



wherein

R¹ and R² are as defined in claim 1,

with a compound of formula III



wherein R³ is as defined in claim 1; or

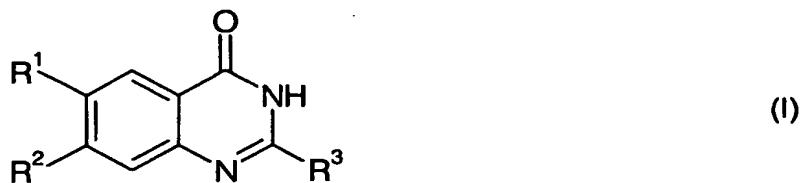
b) for the production of a compound of formula I wherein R³ is NH₂, reacting a compound of formula IV



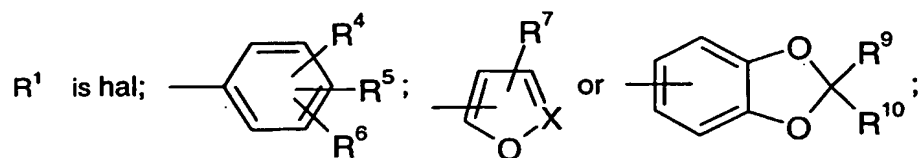
wherein R^1 and R^2 is as defined in claim 1,
 with 2-ethyl-2-thiopseudourea hydrobromide;
 and recovering the obtained compound, in free or in salt form.

7. A compound of any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, for use as a pharmaceutical.

8. A quinazolinone of formula I



wherein



X is N or CR^8 ;

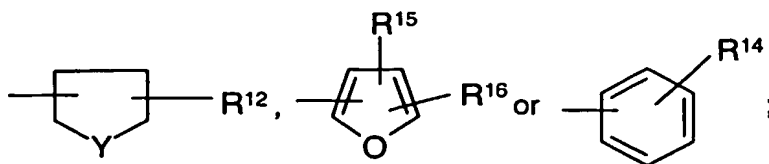
R^2 is hal; nitro; C_1 - C_6 alkylcarbonyl; C_1 - C_6 alkyl or C_3 - C_6 cycloalkyl;

R^3 is C_1 - C_6 alkyl; C_1 - C_6 alkoxy or amino;

R^4 is H; hal; hydroxy; amino; C_1 - C_6 alkyl-amino, di(C_1 - C_6 alkyl)-amino, C_1 - C_6 alkyl; C_1 - C_6 alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkyl; C_3 - C_7 cycloalkyl or C_3 - C_7 cycloalkyl C_1 - C_6 alkoxy that may be substituted at the cycloalkyl residue by C_1 - C_6 alkyl; C_1 - C_6 alkoxycarbonyl; C_3 - C_6 alkenyloxy; $(C_1$ - C_6 alkyl) $_2$ N- C_1 -

C_6 alkoxy; C_1 - C_6 alkyl-sulfanyl; C_1 - C_6 alkyl-sulfanyl C_1 - C_6 alkoxy, or

-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R⁹ and R¹⁰, independently, are H or hal;

R¹¹ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹² is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹³ is H or C₁-C₆alkyl;

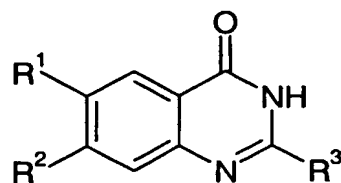
R¹⁴ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl; and

R¹⁵ and R¹⁶, independently, are H; hal; or C₁-C₆alkyl;

in free base or pharmaceutically acceptable acid addition salt form, for use in the treatment or prevention of a disease or condition in which the vanilloid receptor activation plays a role or is implicated.

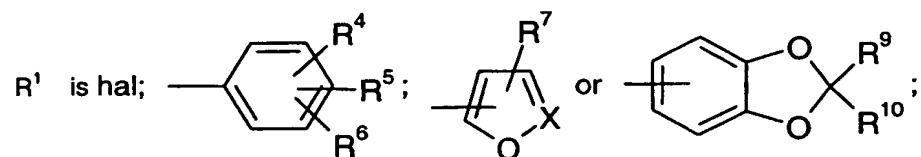
9. A pharmaceutical composition comprising a compound of any one of claims 1 to 4 in free base or pharmaceutically acceptable acid addition salt form, in association with a pharmaceutical carrier or diluent.

10. The use of a quinazolinone of formula I



(I)

wherein



X is N or CR⁸;

R² is hal; nitro; C₁-C₆alkylcarbonyl; C₁-C₆alkyl or C₃-C₆cycloalkyl;

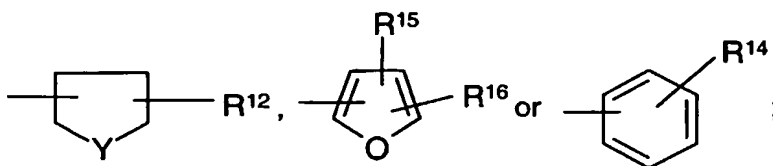
R³ is C₁-C₆alkyl; C₁-C₆alkoxy or amino;

R⁴ is H; hal; hydroxy; amino; C₁-C₆alkyl-amino, di(C₁-C₆alkyl)-amino, C₁-C₆alkyl; C₁-C₆alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkyl; C₃-

C₇cycloalkyl or C₃-C₇cycloalkylC₁-C₆alkoxy that may be substituted at the cycloalkyl residue by C₁-C₆alkyl; C₁-C₆alkoxycarbonyl; C₃-C₆alkenyloxy; (C₁-C₆alkyl)₂N-C₁-

C₆alkoxy; C₁-C₆alkyl-sulfanyl; C₁-C₆alkyl-sulfanylC₁-C₆alkoxy,  or

-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R⁹ and R¹⁰, independently, are H or hal;

R¹¹ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹² is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

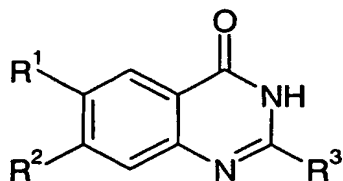
R¹³ is H or C₁-C₆alkyl;

R¹⁴ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl; and

R¹⁵ and R¹⁶, independently, are H; hal; or C₁-C₆alkyl;

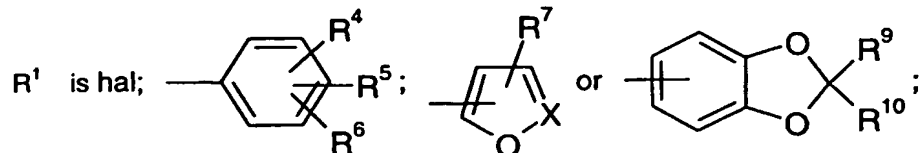
in free base or pharmaceutically acceptable acid addition salt form, as a pharmaceutical for the treatment or prevention of a disease or condition in which vanilloid receptor activation plays a role or is implicated.

11. The use of a quinazolinone of formula I



(I)

wherein



X is N or CR⁸;

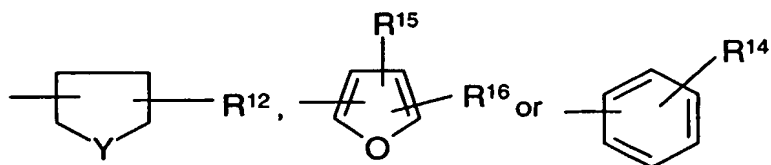
R² is hal; nitro; C₁-C₆alkylcarbonyl; C₁-C₆alkyl or C₃-C₆cycloalkyl;

R³ is C₁-C₆alkyl; C₁-C₆alkoxy or amino;

R⁴ is H; hal; hydroxy; amino; C₁-C₆alkyl-amino, di(C₁-C₆alkyl)-amino, C₁-C₆alkyl; C₁-C₆alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkyl; C₃-C₇cycloalkyl or C₃-C₇cycloalkylC₁-C₆alkoxy that may be substituted at the cycloalkyl residue by C₁-C₆alkyl; C₁-C₆alkoxycarbonyl; C₃-C₆alkenyloxy; (C₁-C₆alkyl)₂N-C₁-

C₆alkoxy; C₁-C₆alkyl-sulfanyl; C₁-C₆alkyl-sulfanylC₁-C₆alkoxy,  or

-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R⁹ and R¹⁰, independently, are H or hal;

R¹¹ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹² is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

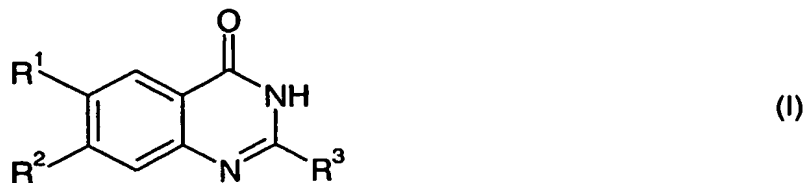
R¹³ is H or C₁-C₆alkyl;

R¹⁴ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl; and

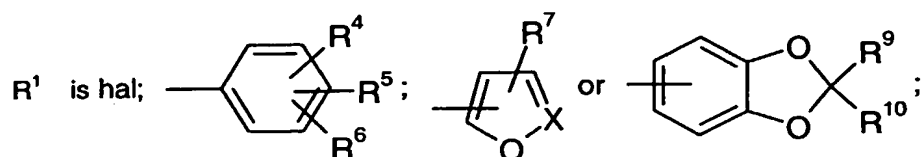
R¹⁵ and R¹⁶, independently, are H; hal; or C₁-C₆alkyl;

in free base or pharmaceutically acceptable acid addition salt form, for the manufacture of a medicament for the treatment or prevention of a disease or condition in which vanilloid receptor activation plays a role or is implicated.

12. A method for treating or preventing a disease or condition in which vanilloid receptor activation plays a role or is implicated comprising administering to a mammal in need thereof a therapeutically effective amount of a quinazolinone of formula I



wherein



X is N or CR⁸;

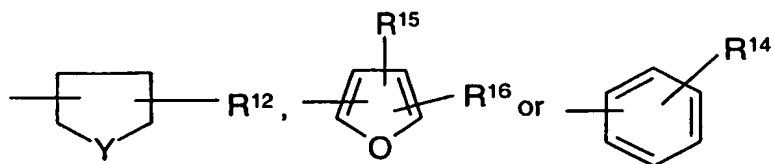
R² is hal; nitro; C₁-C₆alkylcarbonyl; C₁-C₆alkyl or C₃-C₆cycloalkyl;

R³ is C₁-C₆alkyl; C₁-C₆alkoxy or amino;

R⁴ is H; hal; hydroxy; amino; C₁-C₆alkyl-amino, di(C₁-C₆alkyl)-amino, C₁-C₆alkyl; C₁-C₆alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkoxyC₁-C₆alkoxy; C₁-C₆alkoxyC₁-C₆alkyl; C₃-C₇cycloalkyl or C₃-C₇cycloalkylC₁-C₆alkoxy that may be substituted at the cycloalkyl residue by C₁-C₆alkyl; C₁-C₆alkoxycarbonyl; C₃-C₆alkenyloxy; (C₁-C₆alkyl)₂N-C₁-

C₆alkoxy; C₁-C₆alkyl-sulfanyl; C₁-C₆alkyl-sulfanylC₁-C₆alkoxy, or

-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R^9 and R^{10} , independently, are H or hal;

R^{11} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

R^{12} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl;

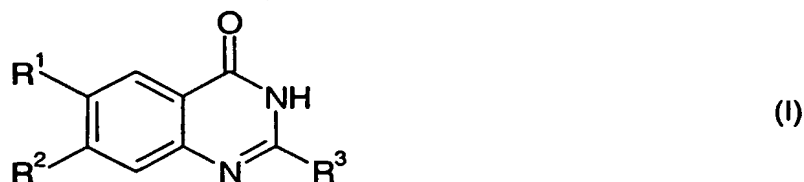
R^{13} is H or C_1 - C_6 alkyl;

R^{14} is H; hal; C_1 - C_6 alkoxy; or C_1 - C_6 alkyl; and

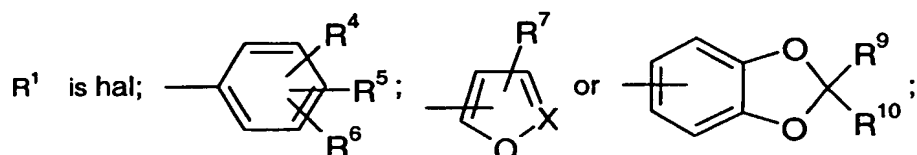
R^{15} and R^{16} , independently, are H; hal; or C_1 - C_6 alkyl;

in free base or pharmaceutically acceptable acid addition salt form.

13. A pharmaceutical composition for the treatment or prevention of a diseases or condition in which vanilloid receptor activation plays a role or is implicated comprising a quinazolinone of formula I



wherein



X is N or CR^8 ;

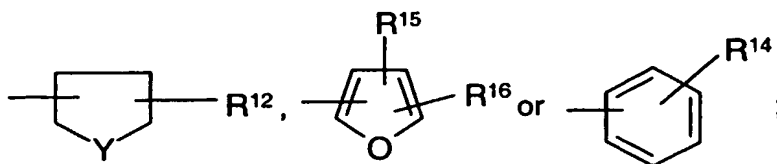
R^2 is hal; nitro; C_1 - C_6 alkylcarbonyl; C_1 - C_6 alkyl or C_3 - C_6 cycloalkyl;

R^3 is C_1 - C_6 alkyl; C_1 - C_6 alkoxy or amino;

R^4 is H; hal; hydroxy; amino; C_1 - C_6 alkyl-amino, di(C_1 - C_6 alkyl)-amino, C_1 - C_6 alkyl; C_1 - C_6 alkoxy which is unsubstituted or mono-, di- or trisubstituted by halogen or hydroxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkoxy C_1 - C_6 alkoxy; C_1 - C_6 alkoxy C_1 - C_6 alkyl; C_3 - C_7 cycloalkyl or C_3 - C_7 cycloalkyl C_1 - C_6 alkoxy that may be substituted at the cycloalkyl residue by C_1 - C_6 alkyl; C_1 - C_6 alkoxycarbonyl; C_3 - C_6 alkenyloxy; (C_1 - C_6 alkyl) $_2$ N- C_1 -



-O-[CH₂]_n-A wherein A represents



Y represents O or NR¹³,

and n is 0, 1, 2, 3, 4, 5 or 6;

R⁵ and R⁶, independently, are H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R⁷ and R⁸, independently, are H or C₁-C₆alkyl;

R⁹ and R¹⁰, independently, are H or hal;

R¹¹ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹² is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl;

R¹³ is H or C₁-C₆alkyl;

R¹⁴ is H; hal; C₁-C₆alkoxy; or C₁-C₆alkyl; and

R¹⁵ and R¹⁶, independently, are H; hal; or C₁-C₆alkyl;

and a carrier.